945-35 ^{18}F-2-deoxyglucose (FDG) Utilization is Regionally Increased in Fasting Pigs with Hibernating Myocardium

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Recent clinical studies with dynamic FDG imaging in fasting patients have shown increased rates of glucose utilization in hibernating myocardium. We sought to determine whether similar findings would be present in pigs with chronically dysfunctional myocardium. Accordingly, we instrumented pigs with a 1.5 mm occluder on the proximal LAD for three months. Dynamic FDG imaging was performed after an overnight fast (n = 9), followed by studies to assess stenosis severity, function and regional perfusion in the closed-chest anesthetized state (n = 7). There was no histological evidence of necrosis. The average LAD stenosis was 94 ± 4% with total occlusion and collaterals in 4 animals. Left ventriculography showed anteroapical hypokinesis or akinesis in each animal (wall motion score = 0.7, normal = 3) with an average ejection fraction of 47 ± 2%. Resting subendocardial perfusion by microspheres was reduced in the LAD territory in comparison to the normally perfused regions of the same animals (0.78 ± 0.09 vs. 0.99 ± 0.06 ml/min/g, $p < 0.05$), and adenosine vasodilator reserve was markedly reduced (1.2 ± 0.2 vs. 4.9 ± 0.4, $p < 0.01$). Fasting blood glucose averaged 122 ± 16 mg/dl. FDG imaging revealed a 1.8 fold increase in accumulation in the LAD region in comparison to the normal regions (0.54 vs. 0.30 μCi/ml, $p < 0.05$). Dynamic analysis confirmed higher rates of glucose utilization (21 ± 4 vs. 11 ± 3 $\mu mol^{-1} \cdot min^{-1} \cdot 100\ g^{-1}$, $p < 0.05$) in the LAD perfusion territory. Thus, this porcine chronic stenosis model exhibits all of the salient features of hibernating myocardium with regional reductions in flow and function in the absence of myocardial necrosis, and increased FDG utilization in the fasting state.

945-36 Increased Myocardial Uptake of 2-Deoxyglucose during Reperfusion: Role of the Translocation of GLUT4

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We have previously observed that myocardial glucose oxidation is increased early during reperfusion. To determine the contribution of increased sarcolemmal glucose transport, myocardial uptake of 2-deoxyglucose (2-DG) and subcellular localization of GLUT4 were determined during reperfusion in hearts perfused with medium containing 0.4 mM palmitate and 8 mM glucose. Hearts were subjected to 20 min of no-flow ischemia, followed by reperfusion for up to 60 min. Transport and phosphorylation of glucose was estimated based on myocardial accumulation of [^{3}H]-2-DG. The ratio of GLUT4 density in sarcolemmal and microsomal membrane fractions (S/M ratio) was determined by Western Blot. After 15 and 60 min of reperfusion the uptake of 2-DG was higher (87 ± 9 and 98 ± 7 nmol/g/min, respectively, $p < 0.05$) as compared to pre-ischemic values (65 ± 1 nmol/g/min). Ischemia elicited translocation of GLUT4 to the sarcolemma (S/M ratio 0.223 ± 0.083 vs. 0.087 ± 0.031 in control hearts, $p < 0.05$). During reperfusion GLUT4 returned gradually to the microsomal pool with S/M 0.180 ± 0.052 and 0.114 ± 0.041 after 15 and 60 min, respectively. In conclusion, translocation of glucose transporters to the plasma membrane may contribute to enhanced glucose uptake early during reperfusion.

945-37 Inhibition of Nitric Oxide Synthesis Prevents Myocardial Stunning Following Repetitive Ischaemia in the Intact Canine Heart

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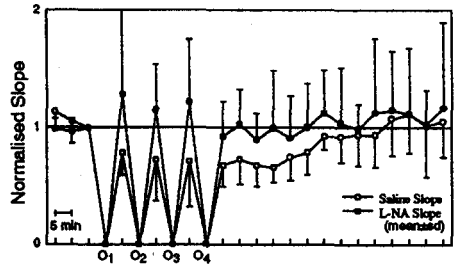
To determine the role of nitric oxide (NO) in the phenomenon of post-ischaemic myocardial stunning, 12 open-chest dogs were instrumented with ultrasonic dimension transducers to measure myocardial segment length in the left anterior descending (LAD) coronary artery territory and a micromanometer to measure LV pressure. LAD blood flow was measured with a Transonic flow probe. Intracoronary infusion of isotonic saline (0.9%) (Control) and N$^{\omega}$-Nitro-L-arginine (L-NA) (30 μg/kg/min), a nitric oxide synthase inhibitor, was performed in two separate groups of 6 dogs each. Data were collected at 5 minute intervals during four 5 minute LAD occlusions (O_X in Figure) separated by 5 minute reperfusions, followed by 60 minutes of final reperfusion. The regional contractile response of the LV was quantified by the slope and length axis-intercept of the stroke work – end-diastolic length (SW-EDL) relationship. In the control group, repetitive ischaemia caused transient depression of the SW-EDL slope (stunning) that resolved over 35 minutes (Figure).



L-NA completely abolished this phenomenon ($p < 0.00001$ by multiple linear regression). No significant post-ischaemic change in SW-EDL intercept was noted in either group. Inhibition of NO synthesis abolished myocardial stunning in this model of repetitive ischaemia.

946 Unstable Angina: Studies of Various Interventions

Monday, March 17, 1997, 3:00 p.m.–5:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 3:00 p.m.–4:00 p.m.

946-1 The Relationship Between Thrombus & Angiographic Outcomes Before & After PTCA in Acute Coronary Syndromes

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The relationship between the presence of thrombus & angiographic outcomes in acute coronary syndromes was examined in pooled data from the RESTORE trial of Tirofiban + heparin vs heparin alone for 36 hrs. post PTCA. The no. of frames for dye to reach standardized distal landmarks were counted to arrive at the previously described Corrected TIMI Frame Count (CTFC), an index of coronary flow. If any thrombus was present (TIMI grade 1–4), the pre-PTCA CTFC was higher (i.e. flow was slower) than if thrombus was absent (37.7 ± 24.9 frames (n = 514) vs 31.2 ± 20.0 (n = 603) ($p < 0.0001$). Patent arteries with thrombus also had tighter minimum lumen diameters (MLD) than arteries without thrombus (0.73 ± 0.39 mm (n = 620) vs 0.80 ± 0.43) (n = 767) (p = 0.002). In a multivariable model of pre-PTCA CTFC, both MLD and thrombus were independently associated with slower pre-PTCA flow ($p < 0.0001$ for both variables). The post PTCA CTFC did not differ between pts. with (17.3 ± 9.8, n = 482) & without thrombus (17.9 ± 10.2, n = 408), nor did the rate of restenosis (54.5% (n = 231) with thrombus vs 53.7% (n = 185) without thrombus). Late loss in MLD was the same in pts. with (0.70 ± 0.77, n = 231) & without thrombus (0.67 ± 0.67, n = 185, p = NS). *Conclusions:* In acute coronary syndromes, arteries with angiographically apparent thrombus have slower flow than arteries without thrombus before PTCA (even in a multivariable model correcting for their tighter MLD) but there was no difference in flow after PTCA. The pre PTCA presence of thrombus was not related to the risk of restenosis nor to the late loss in MLD.

946-2 RV Branch Reperfusion Influences Outcome In RV Infarction

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Whether reperfusion improves acute ischemic RV dysfunction has not been fully delineated. Accordingly, we prospectively studied the responses of the ischemic RV to primary PTCA in 40 pts with acute inferior MI and RV dysfunction by 2D echo manifest by RV free wall (FW) dysfunction and depressed global RV performance. In all cases the RCA was the culprit vessel (pre-PTCA mean stenosis 95 ± 5%, TIMI flow 0.8 ± 0.2). Procedural success was defined as a stenosis < 50% with normalization of flow not only in the main RCA but all RV branches as well. PTCA was successful in 33/40 (83%) pts, 32 (97%) of whom had dramatic immediate recovery of RVFW motion (average of motion score for 3 segments; 1 = normal, 4 = dyskinetic) at 1 hour (2.9 ± 0.7 to 2.0 ± 0.4, *) with further improvement at 3 days (1.4 ± 0.3, *), and complete recovery at 1 week (1.1 ± 0.2, *). Global RV performance, measured by fractional area change (FAC), showed similar immediate improvement at 1 hour (25 ± 8% to 32 ± 5%, *), with further recovery at 3 days (39 ± 7%, *) and 1 week (40 ± 8%, *). PTCA was unsuccessful in 7 pts, although 3 such pts had normal flow to the distal

RCA. Failure of RV branch reperfusion was associated with lack of early recovery of RV wall motion (baseline RVFW motion 3.7 ± 0.4 to 3.3 ± 0.7 at 1 hour and 3.1 ± 0.6 at 1 day) and global RV performance (baseline RV FAC 24 ± 6% to 25 ± 7% at 1 hour and 27 ± 7% at 1 day). Furthermore, in 5 of these 7 (71%) pts, cardiogenic shock developed despite intact LV function (mean LVEF 49 ± 3%) leading to early death within 48 hours in all such cases. These observations demonstrate that primary PTCA resulting in successful RV branch reperfusion leads to prompt and complete recovery of RV performance, and influences clinical outcome. In contrast, inability to restore flow to the RV branches is associated with lack of recovery of RV function and poor clinical outcome. (* $p < 0.05$).

946-3 Predictors of Slowed Non-Culprit Blood Flow Post Thrombolysis

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The presence of abnormally slow flow in non-culprit arteries after thrombolysis has previously been described, & the goal was to determine the relationship between non-culprit flow & other angiographic variables. The frames required for dye to reach standardized distal landmarks were counted, & LAD frame counts were divided by 1.7 to correct for their longer length (Corrected TIMI Frame Count or CTFC). The non-culprit CTFC improved from 32.5 ± 18.1 frames (n = 60) at 60 min. after TNK administration in TIMI 10A to 29.4 ± 13.6 (n = 146) frames at 90 min. ($p = 0.006$), & the 90 min. value was slower than that previously reported for normal arteries in the absence of acute MI (21.0 ± 3.1, n = 78, $p < 0.0001$). Failure to achieve TIMI 3 flow in the culprit artery was associated with slower non-culprit flow at 90 min.: 25.5 ± 11.1 (n = 69) vs 33.1 ± 14.8 frames (n = 75) ($p < 0.001$). Increased normal reference segment diameters in both the non-culprit ($p = 0.007$) & culprit ($p = 0.03$) arteries were both correlated with slower 90 min. non-culprit CTFCs. Left dominant systems were associated with slower non-culprit flow at 90 min.: 36.2 ± 16.3 (n = 20) vs 28.8 ± 13.3 (n = 106), $p = 0.03$. Increased length of the artery distal to the culprit stenosis was correlated with slower non-culprit flow ($p = 0.04$) as was reduced stroke volume ($p = 0.04$) at 90 min. *Conclusions:* These observations confirm the presence of delayed flow in non-culprit arteries at 90 minutes after thrombolysis which appears to be associated with both slower flow in the culprit artery & increased myocardial territory supplied by the culprit artery (i.e. increased arterial diameter & increased artery length distal to the culprit artery stenosis).

946-4 Diagnostic Use of Markers of Myocardial Injury and Intracoronary Thrombus in Patients Presenting to a Emergency Department with Possible Acute Coronary Syndromes

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Varying degrees of intracoronary thrombus formation and myocyte destruction occur in unstable angina (UA) and myocardial infarction (MI). A panel of markers were determined in 99 patients presenting with chest pain thought to be due to possible acute coronary ischemia. This panel included serum for troponin I (TnI), myosin light chain 1 (MLC1), myoglobin (Mb) and spot urine for fibrinopeptide A (FPA) upon presentation and at 4 hours. Patients discharged from the Emergency Department were seen within 48 hours. The final diagnoses determined independent of the study markers were: MI 11 patients, UA 31 patients, stable angina or non-cardiac chest pain 57 patients. Results were (Sensitivity, positive predictive value, negative predictive value and significance, respectively):

	MI		MI or UA	
TnI	91, 100, 99	$p < 0.001$	45, 77, 100	$p < 0.001$
MLC1	91, 21, 98	$p = 0.003$	64, 56, 71	$p = 0.008$
Mb	91, 50, 99	$p < 0.001$	36, 75, 66	$p < 0.001$
FPA	64, 30, 95	$p = 0.003$	36, 65, 66	$p = 0.024$
Any Marker	100, 21, 100	$p < 0.001$	81, 81, 83	$p < 0.001$

Markers of intracoronary thrombus formation and myocyte injury show a high negative predictive value and can differentiate UA and MI patients from other causes of chest pain. Such a panel may impact initial risk assessment and triage options.

946-5 Less Myocardial but More Cerebral Ischemic Events in African Americans Than Caucasians With Acute Coronary Syndromes: Results from GUSTO-II

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Several reports have identified differences between African Americans and Caucasians concerning risk factors and prognosis related to atherosclerotic heart disease, however, data comparing these races with acute coronary syndromes is very limited. Thus, we prospectively collected data regarding outcome and race in the GUSTO-IIB trial which compared outcomes among patients with acute coronary syndromes randomized to heparin or hirudin. The study included 7496 Caucasians and 245 African Americans with ECG evidence of unstable angina or Non-Q-wave MI. Compared to Caucasians, African Americans were younger (57.2 vs 65.9 yrs) but significantly more often female, smokers, hypertensive, and diabetic. Despite this, and presenting later for treatment (6.3 vs 5.0 hrs), African Americans had a similar mortality rate at 30 days (2.9% vs 2.7%). Among survivors, while African Americans were more likely to have cerebral ischemia (stroke), they were less likely to have recurrent myocardial ischemia, refractory ischemia, or MI (table). African Americans were also more likely to undergo PTCA than CABG. These findings confirm important racial differences among patients with acute coronary syndromes, and the independent effect of race is being quantified in a multivariable model.

30-Day Event	African American (%)	Caucasian (%)	p-value
MI	3.8	6.2	0.132
Refractory ischemia	6.3	24.1	< 0.001
CABG	18.9	29.0	0.034
Stroke	6.5	2.0	0.035

946-6 Temporal Distribution of Important ECG Information in Patients with MI: When Should You Take the Next ECG After Lytics?

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ST-segment recovery analysis from continuous 12-lead ECG monitoring has been correlated with infarct artery patency, drug efficacy and clinical outcome. Most hospitals do not yet have continuous 12-lead monitoring capability. To identify the temporal landmarks associated with key ECG changes, all 544 analyzable continuous 12-lead ECG monitor (ST-100, Mortara Instrument) studies from AMI patients treated in the TAMI-9 (n = 196), DUCCS-2 (n = 32), GUSTO-I (n = 217) and IMPACT-I (n = 99) trials were examined. Key ECGs included: PEAK (ECG with most ST deviation); T50 (the first ECG showing 50% recovery suggesting reperfusion); and STEADY (the first ECG showing 50% recovery that is stable for > 4 hours). Key ECGs were timed from: onset of chest pain (CP time); time of the first diagnostic ECG (DX time); and onset of lytic therapy (RX time). Results, as median (25th, 75th %ile) in minutes were:

	PEAK ST	T50	STEADY ST
CP TIME	166 (110, 245)	209 (146, 291)	314 (219, 428)
DX TIME	55 (0, 102)	98 (64, 144)	184 (114, 316)
RX TIME	7.5 (−33, 42)	42 (13, 78)	123 (61, 241)

Thus, despite considerable variability from patient to patient, the sampling from an acute MI population is: 1) about 60 minutes after the first diagnostic ECG for PEAK ST changes 2) about 40 minutes after onset of lytic therapy for first evidence of reperfusion, and 3) about 120 minutes after onset of lytic therapy for stable reperfusion.

946-19 Flow After Adjunctive & Rescue PTCA in TIMI 4 & TIMI 10

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The frames for dye to reach standardized distal landmarks were counted to arrive at the Corrected TIMI Frame Count (CTFC, an index of flow) before & after adjunctive or rescue PTCA following thrombolysis in the TIMI 4 (TPA, APSAC), 10A (TNK), & 10B (TNK, TPA) trials: